IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

10X GENOMICS, INC. and THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY, Plaintiffs, v. PARSE BIOSCIENCES, INC., Defendant.	CIVIL ACTION NO. 22-1117

OPINION

Slomsky, J. **September 14, 2023**

I. INTRODUCTION

On August 24, 2022, Plaintiff 10x Genomics, Inc. ("Plaintiff" or "10x") filed a Complaint along with the Board of Trustees of the Leland Stanford Junior University ("Stanford University") as a nominal defendant[1], against Defendant Parse Biosciences, Inc. ("Defendant" or "Parse") (Doc. No. 1) alleging patent infringement by Defendant. In the Complaint, Plaintiff alleges a claim of patent infringement pursuant to 35 U.S.C. § 271 and seeks a declaratory judgment under 26 U.S.C. §§ 2201, 2202. These claims involve six patents covering genomic technologies: 1) United States Patent No. 10,150,995 ("the '995 patent"); 2) United States Patent No. 10,619,207 ("the '207 patent"); 3) United States Patent No. 10,738,357 ("the '357 patent"); 4) United States Patent No. 10,155,981 ("the '981 patent"); 5) United States Patent No. 10,697,013 ("the '013 patent"); and 6) United States Patent No. 10,240,197 ("the '197 patent") (collectively, "the Asserted Patents").

[1] On October 7, 2022, Stanford University was realigned as Plaintiff. (Doc. No. 9.)

On October 17, 2022, Defendant filed a Motion to Dismiss the Complaint (Doc. Nos. 11-12). Defendant alleges that the Asserted Patents concern ineligible subject matter under 35 U.S.C. § 101. (Doc. No. 12 at 9.) On October 31, 2022, Plaintiff filed a Response (Doc. No. 14), and on November 9, 2022, Defendant filed a Reply (Doc. No. 20).[2] On November 23, 2022, the Court held a hearing on the Motion to Dismiss, and on December 15, 2022, the parties filed supplemental memoranda in support of and in opposition to Defendant's Motion to Dismiss (Doc. Nos. 33. 35). Defendant's Motion (Doc. Nos. 11-12) is now ripe for disposition. For reasons that follow, Defendant's Motion to Dismiss will be denied.

II. FACTUAL BACKGROUND

In the Complaint, Plaintiff alleges that Defendants infringed the six (6) Asserted Patents, which can be grouped into two families. (Doc. No. 12 at 1.) Each group contains three (3) patents. (Id.) The first one includes three patents identified as the "Giresi" patents.[3] The Giresi patents include: 1) United States Patent No. 10,150,995 ("the '995 patent"); 2) United States Patent No. 10,619,207 ("the '207 patent"); and 3) United States Patent No. 10,738,357 ("the '357 patent"). (Id.) The second group includes three patents identified as the "Brenner" patents.[4] The Brenner patents include: 1) United States Patent No. 10,155,981 ("the '981 patent"); 2) United States Patent No.

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[2] This case was originally assigned to the Honorable Maryellen Noreika, United States District Court Judge for the District of Delaware. On November 3, 2022, it was reassigned for all further proceedings to the Honorable Joel H. Slomsky, United States District Court Judge for the Eastern District of Pennsylvania.

[3] Dr. Paul Giresi is listed as an inventor of these three patents. Also listed as an inventor is Dr. Jason Buenrostro. Defendant names the three patents discussed in this section as the "Buenrostro patents," but Plaintiff calls the same group of patents the "Giresi patents." (See Doc. No. 12 at 2; Doc. No. 14 at 1.) Plaintiff also refers to the three patents as the "ATAC-Seq patents." (Doc. No. 33 at 18.) The Court will refer to this group of patents as the "Giresi patents."

[4] Dr. Sydney Brenner is listed as an inventor of this group of three patents.

10,697,013 ("the '013 patent"); and 3) United States Patent No. 10,240,197 ("the '197 patent"). (Id.)

Generally, the Asserted Patents are directed to compositions and laboratory methods used to uncover genetic information that can then be used to better understand the genetic underpinnings of human life and disease. See '981 Patent, Claim 1 ("A method of analyzing nucleic acids from a plurality of single cells . . ."); '013 Patent, Claim 1 ("A method for multiplexed analysis of nucleic acids from single cells . . ."); '197 Patent, Claim 1 ("A method of counting nucleic acids in a sample . . ."); '995 Patent, Claim 1 ("A method for analyzing a biologic sample . . ."); '207 Patent, Claim 1 ("A method for generating a sequencing library from a plurality of cells . . ."); '357 Patent, Claim 1 ("A composition comprising: a permeabilized cell nucleus comprising . . . an insertional enzyme complex . . ."). The Court will address the science relevant to each group of patents seriatim.

A. Scientific Background

A basic overview of the relevant scientific principles is necessary to understand the patent specifications at issue in this case. To begin, every cell in the human body contains chromosomes that encode genetic information. The genetic information encoded in chromosomes is comprised of deoxyribonucleic acids, or "DNA." See '995 Patent at 8:63–9:14, 13:29–35. DNA is a type of molecule known as a "nucleic acid" that can store genetic information. See Defs. Slide 10. Nucleic acids such as DNA are made up of chains of smaller building blocks called nucleotides.[5] https://www.genome.gov/about-genomics/fact-sheets/Deoxyribonucleic-Acid-Fact-Sheet. Each nucleotide in these chains contains one of four nitrogen bases (also known as nucleobases): 1) adenine (A); 2) thymine (T); 3) guanine (G); and 4) cytosine (C). Id. Sequences of nucleotides,

[5] A chain of nucleotides, such as DNA, is also known as a polynucleotide. See Defs. Slide 10.

such as a DNA sequences, provide information that a cell uses to make proteins that constitute much of what is in a living organism, including cells, tissues, enzymes, and antibodies. See Tr. at 102:21–103:6.

When a cell is ready to make proteins, DNA is copied or "transcribed" into a different polynucleotide called messenger RNA ("mRNA"). The mRNA then can be "translated" into a protein. See Tr. at 102:14–20. The specific sequence of nucleotides determines which protein is created. The nucleic acid sequences (i.e., the DNA or RNA sequences) used to make proteins are sometimes referred to as "protein-coding genes." See Tr. at 102:21–103:6.

Not all DNA is used to code for proteins. Much of the human genome consists of "non-coding DNA." This type of DNA helps with other cellular functions such as organizing DNA within a cell and turning genes that do encode for proteins "on or off," a process known as gene expression. Changes in gene expression within a cell by turning protein coding DNA "on or off" are known as epigenetic changes. (See Doc. No. 33 at 17; https://www.cdc.gov/genomics/disease/epigenetics.htm.) Epigenetic changes to DNA control protein coding and gene activity without changing the sequence of DNA.[6] One such epigenetic feature is the wrapping of DNA around compounds known as histones. When DNA is wrapped around a histone, the DNA and histone together form a complex referred to as a nucleosome. In this state, DNA is not accessible for transcription into mRNA and thus cannot be used to make proteins. Tr. at 102:3–103:6; '995 Patent at 12:54–63. Only "open chromatin," parts of DNA that are not wrapped around a histone to create a nucleosome, are available for transcription to mRNA and translation to proteins. Tr. at 102:3–103:6.

[6] In contrast, genetic changes alter the sequence of nucleotides and therefore alter which protein is produced. https://www.cdc.gov/genomics/disease/epigenetics.htm.

Here, the Asserted Patents are focused on compositions and methods that can be used to determine epigenetic features in cells (the Giresi patents), (see Doc. No. 33 at 17; see, e.g., '995 Patent at 21:16–40) and to differentiate between nucleotide (such as DNA) sequences within a large population of cells (the Brenner patents) (see Doc. No. 33 at 17; see, e.g., '981 Patent at 6:33–7:22, 15:36–50).

B. The Giresi Patents

As noted above, the Giresi patents refer to three of the Asserted Patents that Plaintiff alleges were infringed by Defendant. This group of patents includes: 1) the '995 patent; 2) the '207 patent; and 3) the '357 patent. The Giresi patents are directed to unconventional and improved laboratory methods and compositions that enable scientists to uncover genetic information that then can be used to better understand the genetic underpinnings of human life and disease. This vastly improves on conventional methods used by scientists for interrogating open chromatin regions of DNA. (See, e.g., Doc. No. 1 ¶¶ 17, 40.)

The Giresi patents seek to "solve[] problems associated with determining what areas of the genome are available for transcription and translation into proteins—namely regions of open chromatin." (Doc. No. 33 at 18; Tr. at 104:14–105:6.) Prior methods of analyzing areas of open chromatin required a 44-step process that few people could reproduce, a large sample size and extensive time to complete. (Doc. No. 33 at 18; Tr. at 103:12–104:13.) The inventors of the Giresi patents determined that an engineered insertional enzyme, known as a "transposase,"[7] could be

[7] In nature, bacteria (single-cell organisms that, unlike human cells, do not have a nucleus) use transposases to cut pieces of bacterial DNA and transpose them from one part of the bacterial genome to another. See Tr. at 73:3–20. The pieces of DNA cut by the transposase are sometimes called "transposons." Id.

introduced into a cell nucleus and used to tagment only the areas of open chromatin. (See Doc. No. 33 at 18; Tr. at 107:11–108:1; Tr. at 103:12–104:13.) This had never been done before and reduced the 44-step process to a two-step process. (Id.)

In the Giresi patents, the inventors introduced an engineered insertional enzyme called "Tn5 transposase" into cell nuclei to perform tagmentation inside the cell nucleus. Tr. at 106:25–107:3; 106:8–107:20. Previously, tagmentation could only be performed on DNA that had already been removed from the nucleus and stripped from its chromatin complex. Tr. at 76:5–20 & Parse Slide 53. The claims in two of the Giresi patents, the '995 and the '207 Patents, are directed to new applications of the insertional enzyme complex, transposase, by inserting it into a cell nucleus to tagment DNA found in open chromatin to create tagged DNA fragments. (Doc. No. 33 at 20.) The claims in the third patent, the '357 Patent, are directed towards a composition consisting of a man-made insertional enzyme complex (the transposase) and tagged nucleic acid fragments derived from regions of open chromatin located inside the nucleus of a cell. (Doc. No. 33 at 22; '357 Patent, Claim 16.)

C. The Brenner Patents

The Brenner patents refer to another group of three patents that Plaintiff asserts were infringed by Defendant: 1) the '981 patent; 2) the '013 patent; and 3) the '197 patent. The Brenner patents address challenges for analyzing specific nucleic acid sequences within a sample containing a large number of cells. (Doc. No. 33 at 27.) Within such a sample, each cell may have different nucleic acid sequences, resulting in a population containing potentially millions of different nucleic acid sequences. (Id.) Prior methods for analyzing specific nucleic acid sequences in a large sample

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Transposases also can be engineered to include DNA "tags" for use on human DNA. (Doc. No. 33 at 19.) Transposases that include these "tags" are not found in nature. See Tr. at 75:5–21.

provided aggregate results for the population but did not allow for cell-specific analysis. Therefore, these methods could not identify which cell a nucleic acid sequence came from and did not allow scientists to identify variations between cells. (Doc. No. 33 at 28.)

The Brenner patents contain methods allowing scientists to "tag" nucleotide sequences in a way that indicated which cell they were derived from. (Id.) The methods differentiated polynucleotides based on mRNA, using a novel multiplex tagging approach that the inventors termed "MID." (Id.) MID differentiates polynucleotides through a first tag that is associated with the single cell within a sample from which the sample polynucleotide was derived, and a second tag that distinguishes a particular polynucleotide from other sample polynucleotides derived from the same cell. (Id.) Using such methods, it is possible to differentiate between vast numbers of otherwise indistinguishable mRNA sequences in a sample in order to analyze it, and to count the number of different mRNA in each cell. (Id.) This allows measurement of the amount of mRNA in each cell, which shows how much of the corresponding protein that cell is making. (Id.)

The Brenner Patents also disclose a novel method for copying or "reflecting" the MID-tagged polynucleotides—a technique that can be useful when the polynucleotide sequence is long. The inventors termed that method the "reflex method." (Id. at 29.) In sum, the Brenner Patents disclose methods of analysis and counting through MID tagging, and have reflex methods which allows genomes to be sequenced that previously were too long for scientists to fully analyze. (Doc. No. 1 at 15, 40.)

III. STANDARD OF REVIEW

Section 101 of the Patent Act provides that anyone who "invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof" may obtain a patent. 35 U.S.C. § 101. The Supreme Court has recognized three exceptions to the broad categories of subject matter eligible for patenting under § 101: laws

of nature, physical phenomena, and abstract ideas. Alice Corp. Pty. v. CLS Bank Int'l, 573 U.S. 208, 216 (2014). These exceptions "are 'the basic tools of scientific and technological work' that lie beyond the domain of patent protection." Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 569 U.S. 576, 589 (2013) (quoting Mayo Collaborative Servs. v. Prometheus Labs., Inc., 566 U.S. 66, 77-78 (2012)); see also Alice, 573 U.S. at 216. A claim to any one of these exceptions is directed to ineligible subject matter under § 101. "[W]hether a claim recites patent eligible subject matter is a question of law which may contain underlying facts." Berkheimer v. HP Inc., 881 F.3d 1360, 1368 (Fed. Cir. 2018).

Courts follow a two-step "framework for distinguishing patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts." Alice, 573 U.S. at 217; see also Mayo, 566 U.S. at 77-78. First, at step one, the Court determines whether the claims are directed to one of the three patent-ineligible concepts. Alice, 573 U.S. at 217. If the claims are not directed to a patent-ineligible concept, "the claims satisfy § 101 and [the Court] need not proceed to the second step." Core Wireless Licensing S.A.R.L. v. LG Elecs., Inc., 880 F.3d 1356, 1361 (Fed. Cir. 2018). If, however, the Court finds that the claims at issue are directed to a patent-ineligible concept, the Court must then, at step two, search for an "inventive concept" – i.e., "an element or combination of elements that is 'sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself.' " Alice, 573 U.S. at 217-18 (alteration in original) (quoting Mayo, 566 U.S. at 72-73).

A. Step One of the Alice Framework

At step one of Alice, "the claims are considered in their entirety to ascertain whether their character as a whole is directed to excluded subject matter." Internet Patents Corp. v. Active Network, Inc., 790 F.3d 1343, 1346 (Fed. Cir. 2015); see also Affinity Labs of Texas, LLC v.

DIRECTV, LLC, 838 F.3d 1253, 1257 (Fed. Cir. 2016) (step one looks at the "focus of the claimed advance over the prior art" to determine if the claim's "character as a whole" is to ineligible subject matter). In addressing step one of Alice, the Court should be careful not to oversimplify the claims or the claimed invention because, at some level, all inventions are based upon or touch on abstract ideas, natural phenomena, or laws of nature. Alice, 573 U.S. at 217; see also McRO, Inc. v. Bandai Namco Games Am. Inc., 837 F.3d 1299, 1313 (Fed. Cir. 2016). "At step one, therefore, it is not enough to merely identify a patent-ineligible concept underlying the claim; [courts] must determine whether that patent-ineligible concept is what the claim is 'directed to.'" Rapid Litig. Mgmt. Ltd. v. CellzDirect, Inc., 827 F.3d 1042, 1050 (Fed. Cir. 2016).

B. Step Two of the Alice Framework

At step two of Alice, in searching for an inventive concept, the Court looks at the claim elements and their combination to determine if they transform the ineligible concept into something "significantly more." Alice, 573 U.S. at 218; see also McRO, 837 F.3d at 1312. This second step is satisfied when the claim elements "involve more than performance of 'well-understood, routine, [and] conventional activities previously known to the industry.'" Berkheimer, 881 F.3d at 1367 (citation and internal quotation marks omitted); see also Mayo, 566 U.S. at 73. "The inventive concept inquiry requires more than recognizing that each claim element, by itself, was known in the art.... [A]n inventive concept can be found in the non-conventional and non-generic arrangement of known, conventional pieces." Bascom Glob. Internet Servs., Inc. v. AT&T Mobility LLC, 827 F.3d 1341, 1350 (Fed. Cir. 2016). Whether claim elements or their combination are well-understood, routine, or conventional to a person of ordinary skill in the art is a question of fact. Berkheimer, 881 F.3d at 1368.

At both steps of the Alice framework, courts often find it useful "to compare the claims at issue with claims that have been considered in the now considerably large body of decisions applying § 101." TMI Sols. LLC v. Bath & Body Works Direct, Inc., No. 17-965-LPS-CJB, 2018 WL 4660370, at *5 (D. Del. Sept. 28, 2018) (citing Amdocs (Israel) Ltd. v. Openet Telecom, Inc., 841 F.3d 1288, 1294 (Fed. Cir. 2016)); see also Enfish, LLC v. Microsoft Corp., 822 F.3d 1327, 1334 (Fed. Cir. 2016).

IV. ANALYSIS

A. The Claims in the Giresi Patents ('995, '207 and '357) Are Not Directed To Patent Ineligible Concepts Under Step One of the Alice Framework

The claims in the three Giresi patents are eligible for patent protection under 35 U.S.C. § 101.[8] In their Motion to Dismiss (Doc. No. 12), Defendants claim that the Giresi patents are barred from patent protection under § 101 because they are directed to a natural phenomenon. Defendants contend that "[t]he claims of the [Giresi] patents are directed to nothing more than the natural phenomenon that a transposon can and will behave in its normal manner with respect to so-called 'open chromatin.'" (Doc. No. 12 at 10.) They assert that the claims of the Giresi patents are merely inventors hypothesizing "that a commonly used transposon would indeed carry out its previously understood natural function when introduced to chromatin." (Id.; see also Doc. No. 35 at 12-13.) Defendants further argues that any "non-natural components" of the Giresi patents are "routine and conventional," and therefore patent ineligible under § 101. (See Doc. No. 35 at 12-13.) For reasons that follow, the Court disagrees and finds that the Giresi patents are not directed to a natural phenomenon or any other patent-ineligible subject matter.

[8] Section 101 provides: "[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title." 35 U.S.C. § 101.

As noted above, to assess whether a claim is patent eligible, courts engage in a two-step analysis under Alice. Regarding the first step of the Alice framework, the relevant question for the Court is whether the claims are directed to a patent-ineligible subject matter. Internet Patents Corp., 790 F.3d at 1346. Here, the relevant inquiry for the Court is whether the claims in the Giresi patents ('995, '207 and '357) are directed towards a natural phenomenon, as Defendants claim. (See Doc. No. 12 at 10-13; see also Doc. No. 35 at 12-16.) The Court finds that they are not, and therefore are patent eligible.

The court in Illumina found claims patent to be patent eligible where the inventors used "concrete process steps, not merely to observe the presence of the phenomenon that fetal DNA is shorter than maternal DNA, but rather to exploit that discovery in a method for preparation of a mixture enriched in fetal DNA." Illumina, Inc. v. Ariosa Diagnostics, Inc., 967 F.3d 1319, 1326 (Fed. Cir. 2020). Similarly, the court in CellzDirect found the claims in that case to be patent eligible because the claims were "not simply an observation or detection of the ability of hepatocytes to survive multiple freeze-thaw cycles" and were "directed to a new and useful method of preserving hepatocyte cells." Rapid Litig. Mgmt. Ltd. v. CellzDirect, Inc., 827 F.3d 1042, 1048 (Fed. Cir. 2016). Finally, the court in XY found claims to be patent eligible that "improve a laboratory technique for detecting, classifying, and sorting particles from an individual sample, so as to sort each population of particles 'more accurately than in any other separation system'" where the claims employ mathematical formulas with specific flow cytometry limitations. XY, LLC v. Trans Ova Genetics, LC, 968 F.3d 1323, 1328 (Fed. Cir. 2020).

These decisions support the claims in the Giresi patents as being patent eligible. The Giresi patents consist of the three patents: '995, '207 and '357. First, the '995 patent claims are not directed towards a natural phenomenon. The claims of the '995 patent are directed "to

unconventional laboratory methods for analyzing genomic DNA samples by contacting their chromatin regions with an 'insertional enzyme complex' not found in nature to produce tagged nucleic acid molecules not found in nature, and then performing an assay on the tagged nucleic acid molecules to provide sequence information." (Doc. No. 14 at 9.) The referenced insertional enzyme complex is engineered and is not found in nature. (Id.) For example, Claims 1 and 2 of the '995 patent state:

> 1. A method for analyzing a biological sample, comprising:
> (a) contacting chromatin of a genome region of said biological sample with an insertional enzyme complex to produce tagged nucleic acid molecules, wherein said insertional enzyme complex does not comprise an antibody specific to a protein that is part of said chromatin; and
> (b) performing a nucleic acid assay on said tagged nucleic acid molecules or derivatives thereof, to provide sequence information of said tagged nucleic acid molecules or derivatives thereof.
>
> 2. The method of claim 1, further comprising generating a representation of epigenetic features of said genome region at least in part by mapping said sequence information to said genome region.

'995 Patent, Claims 1 & 2. The claims of the '995 patent include references to not only an engineered insertional enzyme complex, but also a method and process for manipulating this complex into the cell nucleus to then generate tagged DNA fragments. (Doc. No. 14 at 9-1; Doc. No. 33 at 20-21.) These are not merely natural phenomena because as in Illumina, this includes "physical process steps that change" the biological sample and does more than merely observing the chromatin region or detecting the presence of that phenomenon. See Illumina, 967 F.3d at 1326; Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 569 U.S. 576, 594–95 (2013). In this regard, "laws of nature and natural phenomena are not patentable, but applications and uses of such laws and phenomena may be patentable. A claim to otherwise statutory subject matter does

not become ineligible by its use of a law of nature or natural phenomenon." Illumina, 967 F.3d at 1324 (citing Diamond v. Diehr, 450 U.S. 175, 187 (1981)); Parker v. Flook, 437 U.S. 584, 590 (1978)). Consequently, the claims of the '995 patent satisfy step one of the Alice framework and are patent eligible.

Second, the claims of the '207 patent also are not directed to a natural phenomenon. The claims of the '207 patent are directed to "unconventional laboratory methods for generating a sequencing library not found in nature using an insertional enzyme complex, specifically a transposase complex, that is also not found in nature." (Doc. No. 14 at 12.) Like the '995 Patent, the '207 Patent laboratory methods achieve more than simply observing a law of nature or detecting the presence of a natural phenomenon. For example, the '207 patent states:

> 1. A method for generating a sequencing library from a plurality of cells, comprising:
>
> a) lysing a plurality of cells to provide a plurality of cell nuclei, wherein the plurality of cell nuclei comprises chromatin;
>
> b) **contacting a cell nucleus of the plurality of cell nuclei with a transposase complex such that polynucleotides of the cell nucleus are tagmented at regions of open chromatin to produce a plurality of tagged fragments**; and
>
> c) performing one or more nucleic acid reactions **on the tagged fragment to produce a sequencing library**.
>
> 2. The method of claim 1, further comprising **sequencing the sequencing library to produce a plurality of sequence reads.**
>
> 19. The method of claim 2, further comprising analyzing the sequence **reads to generate an epigenetic map representing one or more epigenetic features of the polynucleotides of the cell nuclei.**
>
> 22. The method of claim 1, **wherein the transposase complex does not comprise an antibody specific to a protein that is part of chromatin**.

'207 Patent, Claims 1, 2, 19, & 22 (emphasis added). The claims of the '207 patent include references to the man-made transposase complex, a process for contacting the cell nucleus with the transposase so that tagged fragments may be produced, a process for forming a sequencing library using the tagged fragments and creating an epigenetic map representing epigenetic features of cell nuclei. (Doc. No. 14 at 12-13; Doc. No. 33 at 21-22.) As discussed above, these also are not merely natural phenomena. Consequently, the claims of the '207 patent satisfy step one of the Alice framework and are patent eligible.

Finally, the claims of the '357 patent are not directed to a natural phenomenon. The claims of the '357 patent are directed to "unconventional laboratory compositions comprising a non-naturally occurring permeabilized cell nucleus with an insertional enzyme complex and tagged nucleic acid fragments derived from an open-chromatin region with each fragment comprising a first sequencing adapter and a second sequencing adapter." (Doc. No. 14 at 13.) For example, the '357 patent states:

> 16. A composition comprising:
> a permeabilized cell nucleus comprising:
> (a) **an insertional enzyme complex comprising a transposase enzyme**; and
> (b) **a plurality of tagged nucleic acid fragments**, wherein each tagged nucleic acid fragment comprises a first sequencing adapter and a second sequencing adapter **wherein each tagged nucleic acid fragment is derived from a region of open chromatin.**

'357 Patent, Claim 16 (emphases added). The claims of the '357 patent are directed to the man-made composition described in Claim 16. (Doc. No. 14 at 13-14; Doc. No. 33 at 22.) So, as discussed above, this also is not merely a natural phenomenon. Consequently, the claims of the '357 patent satisfy step one of the Alice framework and are patent eligible. As noted above, because all three Giresi patents are not directed to patent-ineligible subject matter and satisfy the first step in the Alice framework, the Court need not reach the second step. See Core Wireless

Licensing S.A.R.L. v. LG Elecs., Inc., 880 F.3d 1356, 1361 (Fed. Cir. 2018). Therefore, the Defendant's motion to dismiss relating to the Giresi patents will be denied.

B. The Claims in the Brenner Patents ('981, '013 and '197) Are Not Directed To Patent Ineligible Concepts Under Step One of the Alice Framework

The claims in the three Brenner patents are also eligible for patent protection under Section 101. In their Motion to Dismiss (Doc. No. 12), Defendants claim that the Brenner patents are barred from patent protection under § 101 because they are directed to the abstract idea of "tagging polynucleotides to keep track of their origin."[9] (Doc. No. 12 at 14-17.) For reasons that follow, the Court disagrees and finds that the Brenner patents are not directed to an abstract idea or any other patent-ineligible subject matter.

Again, as noted above, when deciding whether a claim is patent eligible, courts engage in a two-step analysis under Alice. Under step one of the Alice framework, the Court must decide whether the claims are directed to a patent-ineligible subject matter. Internet Patents Corp., 790 F.3d at 1346. Here, the relevant inquiry for the Court is whether the claims in the Brenner patents ('995, '207 and '357) are directed towards an abstract concept, as Defendants claim. (See Doc. No. 12 at 14-17; see also Doc. No. 35 at 2-7.) The Court finds they are not because laboratory inventions are not abstract ideas. See Illumina, 967 F.3d at 1373; CellzDirect, 827 F.3d at 1048.

[9] In their Motion (Doc. No. 12), Defendants primarily argue that the claims in the Brenner patents must be directed to abstract ideas because, in another lawsuit filed prior to Plaintiff's acquisition of the Brenner patents in which Plaintiff was the defendant, Plaintiff alleged that the patents it was accused of infringing were directed to the abstract idea of "labeling different objects (two or more 'nucleic acid molecules', e.g., portions of DNA) with different labels ('a plurality of nucleic acid label-tags with different sequences')." (Id. at 14.) Defendants claim that Plaintiff's Brenner patents similarly are "directed to the concept of labelling polynucleotides so that one can keep track of where they came from." (Id.) Defendants argues that because these patent claims are allegedly directed to similar abstract concepts, and because Plaintiff has previously argued that such concepts are not patent-eligible under § 101, the Court must find that the Brenner patents at issue here too are patent ineligible. (Id. at 14-17.) For the reasons stated in Section IV(B), the Court disagrees.

The Brenner Patents consist of the three patents: '981, '197 and '013. First, the claims of the '981 patent are not directed to an abstract idea. The '981 patent claims:

> 1. A method of analyzing nucleic acids from a plurality of single cells, the method comprising:
>
> (a) providing a sample comprising a plurality of single cells, wherein each single cell of the plurality of single cells comprises a plurality of sample polynucleotides;
>
> (b) generating a plurality of tagged polynucleotides from the plurality of sample polynucleotides, wherein each tagged polynucleotide comprises:
>
> (i) a sequence from a sample polynucleotide of the plurality of sample polynucleotides; and
>
> (ii) a multiplex identifier (MID) sequence comprising:
>
> I. a first tag sequence associated with the single cell from which the sample polynucleotide is derived, wherein the first tag sequence is a different sequence for different single cells in the plurality of single cells; and
>
> II. a second tag sequence distinguishing the sample polynucleotide from other sample polynucleotides derived from the same single cell;
>
> (c) sequencing the plurality of tagged polynucleotides to obtain a plurality of identified polynucleotide sequences;
>
> (d) using the first tag sequence to correlate the identified polynucleotide sequence with the single cell from which the identified polynucleotide sequence is derived; and
>
> (e) using the second tag sequence to correlate the identified polynucleotide sequence with the sample polynucleotide from which the identified polynucleotide sequence is derived.

(Doc. No. 14 at 18; see also '981 Patent, Claim 1.) Thus, claim 1 of the '981 Patent is directed to methods of analyzing nucleic acids within a population of cells that require not only the physical step of "generating a plurality of tagged polynucleotides" comprising "a multiplex identifier (MID) sequence," but also the physical step of "sequencing the tagged polynucleotides" to obtain a plurality of identified polynucleotide sequences. (Doc. No. 33 at 31.) Further, several of the

dependent claims add additional physical, non-abstract steps, including "amplifying the tagged polynucleotides prior to the sequencing step" (claim 2) and generating the tagged nucleotides "through at least one ligation reaction" (claim 5). (Id.) Consequently, the claims in '981 are not directed to an abstract concept.

Second, the claims of the '197 and '013 patents also are not directed to an abstract concept. Rather, they cover methods for identifying "correlation between a polynucleotide and its source" so that researchers can know how many individual polynucleotides are in each single cell within a sample. (Id. at 31.) For example, the '197 patent claims:

> 1. A method of counting nucleic acids in a sample, the method comprising:
>
> (a) providing a sample comprising a plurality of cells, wherein a cell of the plurality of cells comprises a plurality of sample polynucleotides;
>
> (b) generating a plurality of tagged polynucleotides from the plurality of sample polynucleotides of said cell and a plurality of oligonucleotide tags, wherein a tagged polynucleotide of the plurality of tagged polynucleotides comprises:
>
> (i) a sample sequence from a sample polynucleotide of the plurality of sample polynucleotides;
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> (ii) a first tag sequence distinguishing said sample polynucleotide from sample polynucleotides from other cells; and
>
> (iii) a second tag sequence distinguishing said sample polynucleotide from other sample polynucleotides from said cell;
>
> (c) sequencing the tagged polynucleotide to determine the sample sequence, the first tag sequence, and the second tag sequence; and
>
> (d) using the first tag sequence and the second tag sequence to count a number of sample polynucleotides in said plurality of sample polynucleotides of said cell.

'197 Patent, Claim 1. Similarly, The '013 Patent claims:

> 1. A method for multiplexed analysis of nucleic acids from single cells, the method comprising:

> (a) providing a sample comprising a plurality of cells, wherein a single cell of the plurality of cells comprises a plurality of sample polynucleotides;
> (b) performing combinatorial tagging to generate a plurality of tagged polynucleotides from said plurality of sample polynucleotides and a plurality of oligonucleotide tags, wherein a tagged polynucleotide of the plurality of tagged polynucleotides is generated by:
>
> (A) providing an extension product by primer extension using a first oligonucleotide tag and a sample polynucleotide of said plurality of sample polynucleotides, and
> (B) ligating a second oligonucleotide tag to said extension product, and wherein said tagged polynucleotide of the plurality of tagged polynucleotides comprises:
>
> (i) a sample sequence corresponding to said sample polynucleotide of the plurality of sample polynucleotides;
> (ii) a first tag sequence distinguishing said sample polynucleotide from sample polynucleotides from other cells; and
> (iii) a second tag sequence distinguishing said sample polynucleotide from other sample polynucleotides from said cell;
>
> (c) amplifying said tagged polynucleotide, thereby generating a plurality of amplified polynucleotides corresponding to the tagged polynucleotide; and
> (d) sequencing said plurality of amplified polynucleotides to determine sequences of the amplified polynucleotides corresponding to the sample sequence, the first tag sequence, and the second tag sequence of the tagged polynucleotide; and
> (e) using the sequences determined in step (d) to count sample polynucleotides for multiple different sample polynucleotides of multiple different single cells of said plurality of cells.

'013 Patent, Claim 1. Thus, the claims in the Brenner Patents cover methods that allow for the generation of combinatorically-tagged polynucleotides that may be used for further research and analysis.

These claims are not directed to an abstract idea. The physical steps of the above claimed methods, including "providing an extension product by primer extension," "ligating . . . to said extension product," "amplifying said tagged polynucleotide, thereby generating a plurality of amplified polynucleotides," and "sequencing," are not directed to an abstract idea. Overall, the Brenner Patents' claims of tagging each polynucleotide with a first tag sequence and a second tag sequence is not merely the allegedly abstract idea of labeling a polynucleotide. Rather, the claims govern methods that differentiate previously undifferentiable pools of polynucleotides within a population of cells and count each distinct polynucleotide within each cell. (Id. at 30.)

As noted above, because all three Brenner patents are not directed to patent-ineligible subject matter and satisfy the first step in the Alice framework, the Court need not reach the second step. See Core Wireless Licensing S.A.R.L. v. LG Elecs., Inc., 880 F.3d 1356, 1361 (Fed. Cir. 2018). Therefore, the Defendant's motion to dismiss relating to the Brenner patents will be denied.

V. CONCLUSION

For the reasons stated above, Defendant's Motion to Dismiss (Doc. No. 12) will be denied. An appropriate Order will follow.